

Appl. No. 09/975,317  
Amendment dated: November 16, 2004  
Reply to OA of: July 16, 2004

### **REMARKS**

Applicants have amended the claims to more particularly define the invention taking into consideration the outstanding Official Action which has withdrawn all the previous rejections and issued new grounds of rejection. Applicants have canceled all the claims in the application and replaced them with new claims 75-95. New claim 75 corresponds to canceled claim 68. Canceled claim 68 was only rejected on the grounds of anticipation under 35 U.S.C. 102(b) with respect to the Rocklage U.S. Patent 5,190,744. Therefore, the rejection of claims 59-62 under 35 U.S.C. 103 as being unpatentable over Rocklage 5,190,744 in view of Rocklage 4,889,931 has been obviated by Applicants' amendments to the claims.

This is similarly true with respect to the rejection of claim 54 as being unpatentable over Rocklage in view of Goldenberg. Accordingly, in view of the amendments to the claims, it is most respectfully requested that these rejections be withdrawn.

Claims 52-63 have been simply rewritten as claims 76-87 with the corresponding dependencies as formerly presented. All of these claims are either directly or indirectly dependent upon claim 75.

Claims 64 and 67 have been rewritten as claims 94 and 95 and are independent claims.

Claims 69-74 have been rewritten as claims 88-93 and the corresponding dependencies of these claims have been amended to be proper dependent claims. Applicants most respectfully submit that all the claims now present in the application, claims 75-95 are in full compliance with 35 U.S.C. 112 and are clearly patentable over the references of record.

Appl. No. 09/975,317  
Amendment dated: November 16, 2004  
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As noted above, all of the prior art rejections have been obviated by the amendments to the claims except for the rejection of claims 51-53, 55-58 and 63-74 as being anticipated under 35 U.S.C. 102(b) by Rocklage U.S. 5,190,744.

Applicants wish to direct the Examiner's attention to MPEP § 2131 which states that to anticipate a claim, the reference must teach every element of the claim.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed.Cir. 1990).

In the Official Action it is urged that Rocklage discloses a method of detecting myocardial ischemia in a subject comprising administering a contrast media comprising a manganese complex and subjecting the subject to a fast MRI technique to detect abnormal blood flow. Specific reference is made to the abstract.

In addition, it is urged in the Official Action that methods of fast MRI, as claimed are disclosed in column 2, lines 10+ and manganese chelates are disclosed with a reference to column 4, line 55 and claim 26.

The specific dosages are said to be within the claim limits. It is urged that since the chelates are used, as encompassed by the instant claims, the middle complexes thereof would inherently be expected to have the same values as claimed. The contrast agents include pharmaceutical compositions containing calcium complexes, buffers, antioxidants, etc. as claimed with reference to column 6. This rejection having been carefully considered is most respectfully traversed in view of the amendments to the claims even though claim 68 included in the rejection has not been further amended.

Appl. No. 09/975,317  
Amendment dated: November 16, 2004  
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Accordingly, the rejection with respect to all the claims remaining in the application is specifically traversed.

More particularly, Applicants wish to point out that the method claimed in claim 75 is not the same as the method described in Rocklage '744. Firstly, the present invention relates to the detection of myocardial ischemia whereas Rocklage '744 is concerned with the detection of cerebral (brain) ischemia. Although Rocklage '744 also teaches that the same method would be useful in the detection of coronary ischemia, the myocardium and coronary arteries are different parts of the heart - the myocardium is the middle muscular layer of the heart wall, and coronary arteries surround the heart and branch out from the aorta to supply blood to the heart. Rocklage '744 does not therefore describe a method of detecting myocardial ischemia as in the presently claimed invention.

Secondly, the specific method claimed in claim 75 can be further distinguished from the prior art. Rocklage '744 does not disclose a method of distinguishing between reversibly injured tissue and irreversibly injured tissue. It describes only a method for detecting ischemia. Ischemia is a decrease of blood supply which leads to an inadequate supply of oxygen where the blood supply is limited. The contrast agents described in Rocklage '744, in particular the Dy-compounds described in the Examples of '744, are blood pool agents and are detected in the blood supply by MRI. As a result, the method described in Rocklage '744 can only be used to identify and/or monitor abnormal or modified blood flow. The method does not involve or allow for the detection of damaged tissue.

On the other hand, independent claim 75 of the present application is directed to a method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue. Ischemia leads to the damage of tissue to which the patient's blood supply has been affected. The extent of the tissue damage within a patient can vary such that the damage to some tissue is reversible, whereas the damage to other tissue is not. Claim 75 is limited to a method for distinguishing between these types of tissue

following/during an ischemic event. Such a method is nowhere disclosed or suggested in Rocklage '744.

The method claimed in the present application relies on the contrast agent used being able to distinguish between reversibly and irreversibly injured myocardial tissue. This is achieved using the contrast agents defined in the claims. The manganese contrast agents described in the present application dissociate once they have been administered into the body and the resulting manganese ions are able to enter viable (i.e. repairable) myocardial cells via  $\text{Ca}^{2+}$  channels. It should be noted that not all metal ions are capable of being taken up by cells via  $\text{Ca}^{2+}$  channels. The manganese ions are not however able to enter myocardial cells which are irreversibly damaged. The manganese ions generate a signal in MRI imaging, thereby generating a signal in the viable myocardial cells. Since manganese ions cannot be taken up by irreversibly damaged cells, no such signal is generated in necrotic (infarcted) cells. The method claimed in present claim 75 is therefore able to distinguish between the two types of cells. Rocklage '744 does refer to manganese ions. However, this reference forms part of the general teaching provided by the document. The reference to manganese ions in Rocklage '744 cannot be considered prejudicial to the novelty of the claims since Rocklage '744 does not disclose a method for distinguishing between reversibly and irreversibly injured myocardial tissue as discussed above. It should be noted that only Dy-contrast agents are employed in the Examples of Rocklage '744, and Dy-contrast agents are not suitable for detecting the viability of myocardial cells. This is because Dy-contrast agents are taken up neither by viable myocardial cells nor by irreversibly damaged myocardial cells. Consequently, a method employing such contrast agents is not able to distinguish between the two types of cells.

The method as claimed in claim 75 can therefore be distinguished from the methods described in the prior art. Furthermore, it is submitted that the claimed method is not obvious since a method for distinguishing repairable myocardial cells from irreparable cells is nowhere disclosed in the prior art. None of the prior art documents even address the problem of distinguishing repairable cells from irreparable cells.

Appl. No. 09/975,317  
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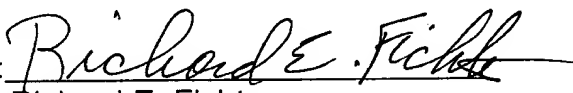
Furthermore, neither is there anything in the prior art to suggest that manganese contrast agents would dissociate when administered to a patient, nor that the resulting manganese ions would be taken up by viable myocardial tissue and not by necrotic tissue. The skilled person would not therefore be led to the claimed method from the cited prior art. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The above comments equally apply to claims 94 (corresponding to canceled claim 64) and 95 (corresponding to canceled claim 67) and therefore it is most respectfully requested that for the same reasons as discussed above, these rejections be withdrawn.

In view of the above comments and further amendments to the claims, favorable reconsideration and allowance of all of the claims now present in the application are most respectfully requested.

Respectfully submitted,

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